CLAIMS

1. A method for generating multiple RNA copies comprising the steps of:

(a) providing a sample comprising target RNA, wherein said sample is simultaneously contacted with:

- an oligonucleotide comprising at its 5' side a promoter sequence recognized by an RNA polymerase, wherein each oligonucleotide further comprises a target hybridising sequence, which is a random sequence; and
- an enzyme having DNA polymerase activity;
- an enzyme having RNase H activity;
- an enzyme having RNA polymerase activity; and,
- sufficient amounts of nucleotides; and,

(b) maintaining the resulting reaction mixture under the appropriate conditions for a sufficient amount of time for the enzymatic processes to take place.

2. A method for generating multiple RNA copies comprising the steps of:

(a) providing a sample comprising target RNA, wherein said sample is simultaneously contacted with:

- a DNA oligonucleotide comprising at its 5' side a promoter sequence recognized by an RNA polymerase, wherein each oligonucleotide further comprises a target hybridising sequence, which is a predetermined sequence; and,
- an enzyme having Klenow pol I exo (-) activity;
- an enzyme having RNase H activity;
- an enzyme having RNA polymerase activity; and,
- sufficient amounts of nucleotides; and,

(b) maintaining the resulting reaction mixture under the appropriate conditions for a sufficient amount of time for the enzymatic processes to take place.

3. A method for generating multiple RNA copies comprising the steps of:

(a) providing a sample comprising target RNA; wherein said sample is simultaneously contacted with:

- an oligonucleotide comprising at its 5' side a promoter sequence recognized by an RNA polymerase, wherein each oligonucleotide further comprises:

- a target hybridising sequence, wherein said hybridising sequence is a predetermined sequence,
- a modified nucleotide at its 3' terminal end in such a way that extension therefrom is prohibited,
- at least one chimeric linkage between nucleotides at the 3' end; and,
- an enzyme having DNA polymerase activity;
- an enzyme having RNase H activity;
- an enzyme having RNA polymerase activity; and,
- sufficient amounts of nucleotides; and,

(b) maintaining the resulting reaction mixture under the appropriate conditions for a sufficient amount of time for the enzymatic processes to take place.

4. The method according to any of claims 1 to 3, wherein said target RNA is of eukaryotic, prokaryotic or viral origin, or a mixture thereof.

5. The method according to any of claims 1 to 4, wherein said target RNA is chosen from the group comprising total RNA, mRNA, cRNA, rRNA, tmRNA, asRNA, hnRNA or tRNA, including any combination thereof.

6. The method according to any of claims 2 to 5, wherein said predetermined sequence is chosen from the group comprising gene-specific sequences, viral sequences, prokaryotic sequences, mutation-specific sequences, poly-T sequences, genomic sequences and rRNA.

7. The method according to any of claims 3 to 6, wherein said modified nucleotide is chosen from the group comprising nucleotides comprising alkane-diol residues, cordycepins, amino-alkyls, and dideoxynucleotides.

8. The method according to any of claims 1 to 7, wherein at least one of the nucleotides, e.g. dNTPs and rNTPs, is provided with a label.

9. The method according to any of claims 1 to 8, wherein the generated RNA is used as input material for further amplification.

10. The method according to any of claims 1 to 9, wherein the generated RNA is contacted with:

- an RNA ligase,
- a double stranded nucleic acid complex comprising a double stranded DNA promoter sequence that can be recognized by an RNA polymerase, whereby one strand of said complex has a stretch of RNA attached to the 5' end of one of the DNA strands,
- an enzyme having RNA polymerase activity, and
- sufficient amounts of dNTPs and rNTPs;

wherein the resulting reaction mixture is maintained under the appropriate conditions for a sufficient amount of time for the enzymatic processes to take place.

11. The method according to any of claims 1 to 10, wherein the reaction mixture further comprises:

- an RNA ligase; and,
- a double stranded nucleic acid complex comprising a double stranded DNA promoter sequence that can be recognized by the RNA polymerase, whereby one strand of said complex has a stretch of RNA attached to the 5' end of one of the DNA strands.

12. The method according to any of claims 1 to 11, wherein the generated RNA copies are contacted with poly A polymerase.

13. The method according to any of the claims 1 to 12, wherein the starting material is simultaneously contacted with a poly A polymerase.

14. The method according to claim 10 or 11, wherein the stretch of RNA attached to the 5' end of one of the DNA strands is phosphorylated at the 5' end.

15. The method according to any of claims 1 to 14, wherein said promoter sequence is a T7 promoter sequence.

16. The method according to any of claims 1 to 15, wherein said RNA polymerase is a T7 RNA polymerase.

17. The method according to any of claims 1 and 3 to 16, wherein said enzyme having DNA polymerase activity is AMV-RT or MMLV-RT.

18. The method according to any of claims 1 to 17, wherein said enzyme having RNase H activity is *E. coli* RNase H .

19. The method according to any of claims 1 to 17, wherein said enzyme having RNase H activity is reverse transcriptase.

20. The method according to claim 19, wherein said enzyme having RNase H activity is AMV-RT or MMLV-RT.

21. A method for determining differences in gene expression in cell samples, comprising the steps of:

- creating multiple RNA copies of one or more target RNA species according to the method of any of claims 1 to 20, whereby a first pattern of expression is formed from the sample;
- comparing said first pattern of expression with a predetermined pattern of expression, whereby differences in gene expression are determined.

22. The method according to any of claims 1 to 21, wherein said multiple RNA copies are used to interrogate a probe array.

23. The method according to claim 22, wherein said probe array is an oligonucleotide array.

24. Kit for generating multiple RNA copies comprising:

- an oligonucleotide comprising at its 5' side a promoter sequence recognized by an RNA polymerase, wherein each oligonucleotide further comprises a target hybridising sequence, which is a random sequence or a predetermined sequence, and possibly a modification at its 3' terminal end in such a way that extension therefrom is prohibited; and,
- possibly, an enzyme having DNA polymerase activity;

- possibly, an enzyme having RNase H activity;
- possibly, an enzyme having RNA polymerase activity;
- possibly, sufficient amounts of dNTPs and rNTPs, and
- instructions to carry out the method for generating multiple RNA copies.

25. The kit according to claim 24, further comprising:
- an RNA ligase, and
- a double stranded nucleic acid complex comprising a double stranded DNA promoter sequence that can be recognized by an RNA polymerase, whereby one strand of said complex has a stretch of RNA attached to the 5' end of one of the DNA strands,
- instructions to carry out further amplification.

26. The kit according to claim 24 or 25, further comprising a probe array, and possibly instructions to interrogate the array.